

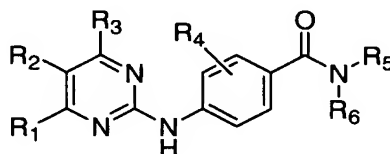
Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of claims

What is claimed is:

1. (Previously Presented) A method for treating a condition responsive to inhibition of the JNK pathway, comprising administering to a patient in need thereof an effective amount of a compound having the structure:



or a pharmaceutically acceptable salt thereof,

wherein:

R₁ is aryl or heteroaryl optionally substituted with one to four substituents independently selected from R₇;

R₂ and R₃ are the same or different and are independently hydrogen or lower alkyl;

R₄ represents one to four optional substituents, wherein each substituent is the same or different and independently is selected from halogen, hydroxy, lower alkyl or lower alkoxy;

R₅ and R₆ are the same or different and independently are -R₈, -(CH₂)_aC(=O)R₉, -(CH₂)_aC(=O)OR₉, -(CH₂)_aC(=O)NR₉R₁₀, -(CH₂)_aC(=O)NR₉(CH₂)_bC(=O)R₁₀, -(CH₂)_aNR₉C(=O)R₁₀, -(CH₂)_aNR₁₁C(=O)NR₉R₁₀, -(CH₂)_aNR₉R₁₀, -(CH₂)_aOR₉, -(CH₂)_aSO_cR₉, or -(CH₂)_aSO₂NR₉R₁₀;

or R₅ and R₆ taken together with the nitrogen atom to which they are attached to form a heterocycle or substituted heterocycle;

R₇ is at each occurrence independently halogen, hydroxy, cyano, nitro, carboxy, alkyl, alkoxy, haloalkyl, acyloxy, thioalkyl, sulfinylalkyl, sulfonylalkyl, hydroxyalkyl, aryl, substituted aryl, aralkyl, substituted aralkyl, heterocycle, substituted heterocycle, heterocyclealkyl, substituted heterocyclealkyl, -C(=O)OR₈, -OC(=O)R₈, -C(=O)NR₈R₉, -C(=O)NR₈OR₉, -SO_cR₈, -SO_cNR₈R₉, -NR₈SO_cR₉, -NR₈R₉, -NR₈C(=O)R₉,

$-\text{NR}_8\text{C}(=\text{O})(\text{CH}_2)_b\text{OR}_9$, $-\text{NR}_8\text{C}(=\text{O})(\text{CH}_2)_b\text{R}_9$, $-\text{O}(\text{CH}_2)_b\text{NR}_8\text{R}_9$, or heterocycle fused to phenyl;

R_9 , R_{10} and R_{11} are the same or different and at each occurrence are independently hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, aralkyl, substituted arylalkyl, heterocycle, substituted heterocycle, heterocyclealkyl or substituted heterocyclealkyl;

R_8 is aryl, substituted aryl, aralkyl, substituted arylalkyl, heterocycle, substituted heterocycle, heterocyclealkyl or substituted heterocyclealkyl;

or R_8 and R_9 taken together with the atom or atoms to which they are attached to form a heterocycle or substituted heterocycle;

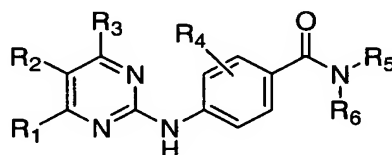
a and b are the same or different and at each occurrence independently are selected from 0, 1, 2, 3 or 4; and

c is at each occurrence 0, 1 or 2,

wherein the condition is atherosclerosis, restenosis following angioplasty, left ventricular hypertrophy, Type II diabetes, osteoporosis, erectile dysfunction, cachexia, myocardial infarction, ischemic diseases of heart, kidney, liver, and brain, organ transplant rejection, graft versus host disease, endotoxin shock, or multiple organ failure.

2-16. (Canceled)

17. (Currently Amended) A method for treating a condition comprising administering to a patient in need thereof an effective amount of a compound having the structure:



or a pharmaceutically acceptable salt thereof,

wherein:

R_1 is aryl or heteroaryl optionally substituted with one to four substituents independently selected from R_7 ;

R_2 and R_3 are the same or different and are independently hydrogen or lower alkyl;

R₄ represents one to four optional substituents, wherein each substituent is the same or different and independently selected from halogen, hydroxy, lower alkyl or lower alkoxy;

R₅ and R₆ are the same or different and independently are -R₈, -(CH₂)_aC(=O)R₉, -(CH₂)_aC(=O)OR₉, -(CH₂)_aC(=O)NR₉R₁₀, -(CH₂)_aC(=O)NR₉(CH₂)_bC(=O)R₁₀, -(CH₂)_aNR₉C(=O)R₁₀, -(CH₂)_aNR₁₁C(=O)NR₉R₁₀, -(CH₂)_aNR₉R₁₀, -(CH₂)_aOR₉, -(CH₂)_aSO_cR₉, or -(CH₂)_aSO₂NR₉R₁₀;

or R₅ and R₆ taken together with the nitrogen atom to which they are attached to form a heterocycle or substituted heterocycle;

R₇ is at each occurrence independently halogen, hydroxy, cyano, nitro, carboxy, alkyl, alkoxy, haloalkyl, acyloxy, thioalkyl, sulfinylalkyl, sulfonylalkyl, hydroxyalkyl, aryl, substituted aryl, aralkyl, substituted aralkyl, heterocycle, substituted heterocycle, heterocyclealkyl, substituted heterocyclealkyl, -C(=O)OR₈, -OC(=O)R₈, -C(=O)NR₈R₉, -C(=O)NR₈OR₉, -SO_cR₈, -SO_cNR₈R₉, -NR₈SO_cR₉, -NR₈R₉, -NR₈C(=O)R₉, -NR₈C(=O)(CH₂)_bOR₉, -NR₈C(=O)(CH₂)_bR₉, -O(CH₂)_bNR₈R₉, or heterocycle fused to phenyl;

R₉, R₁₀ and R₁₁ are the same or different and at each occurrence are independently hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, aralkyl, substituted arylalkyl, heterocycle, substituted heterocycle, heterocyclealkyl or substituted heterocyclealkyl;

R₈ is aryl, substituted aryl, aralkyl, substituted arylalkyl, heterocycle, substituted heterocycle, heterocyclealkyl or substituted heterocyclealkyl;

or R₈ and R₉ taken together with the atom or atoms to which they are attached to form a heterocycle or substituted heterocycle;

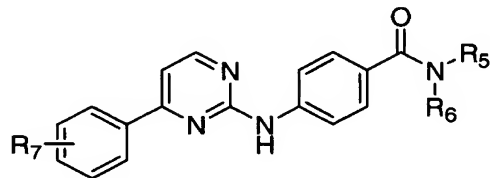
a and *b* are the same or different and at each occurrence independently selected from 0, 1, 2, 3 or 4; and

c is at each occurrence 0, 1 or 2,

wherein the condition is ~~atherosclerosis, restenosis following angioplasty, left ventricular hypertrophy, Type II diabetes, osteoporosis, erectile dysfunction, cachexia, myocardial infarction,~~ ischemic diseases of heart, kidney, liver, and or brain, ~~organ transplant rejection, graft versus host disease, endotoxin shock, or multiple organ failure.~~

18-26. (Canceled)

27. (Currently Amended) A method for treating a condition comprising administering to a patient in need thereof an effective amount of a compound having the structure:



or a pharmaceutically acceptable salt thereof,

wherein:

R_5 and R_6 are the same or different and independently are $-R_8$, $-(CH_2)_aC(=O)R_9$, $-(CH_2)_aC(=O)OR_9$, $-(CH_2)_aC(=O)NR_9R_{10}$, $-(CH_2)_aC(=O)NR_9(CH_2)_bC(=O)R_{10}$, $-(CH_2)_aNR_9C(=O)R_{10}$, $-(CH_2)_aNR_{11}C(=O)NR_9R_{10}$, $-(CH_2)_aNR_9R_{10}$, $-(CH_2)_aOR_9$, $-(CH_2)_aSO_cR_9$, or $-(CH_2)_aSO_2NR_9R_{10}$;

or R_5 and R_6 taken together with the nitrogen atom to which they are attached to form a heterocycle or substituted heterocycle;

R_7 is at each occurrence independently halogen, hydroxy, cyano, nitro, carboxy, alkyl, alkoxy, haloalkyl, acyloxy, thioalkyl, sulfinylalkyl, sulfonylalkyl, hydroxyalkyl, aryl, substituted aryl, aralkyl, substituted aralkyl, heterocycle, substituted heterocycle, heterocyclealkyl, substituted heterocyclealkyl, $-C(=O)OR_8$, $-OC(=O)R_8$, $-C(=O)NR_8R_9$, $-C(=O)NR_8OR_9$, $-SO_cR_8$, $-SO_cNR_8R_9$, $-NR_8SO_cR_9$, $-NR_8R_9$, $-NR_8C(=O)R_9$, $-NR_8C(=O)(CH_2)_bOR_9$, $-NR_8C(=O)(CH_2)_bR_9$, $-O(CH_2)_bNR_8R_9$, or heterocycle fused to phenyl;

R_8 , R_9 , R_{10} and R_{11} are the same or different and at each occurrence are independently hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, aralkyl, substituted arylalkyl, heterocycle, substituted heterocycle, heterocyclealkyl or substituted heterocyclealkyl;

or R_8 and R_9 taken together with the atom or atoms to which they are attached to form a heterocycle or substituted heterocycle;

a and b are the same or different and at each occurrence independently selected from 0, 1, 2, 3 or 4; and

c is at each occurrence 0, 1 or 2,

wherein the condition is ~~atherosclerosis, restenosis following angioplasty, left ventricular hypertrophy, Type II diabetes, osteoporosis, erectile dysfunction, cachexia,~~

~~myocardial infarction, ischemic diseases of heart, kidney, liver, and or brain, organ transplant rejection, graft versus host disease, endotoxin shock, or multiple organ failure.~~

28. (Previously Presented) The method of claim 1, wherein the condition is atherosclerosis, restenosis following angioplasty, left ventricular hypertrophy, erectile dysfunction or myocardial infarction.

29. (Previously Presented) The method of claim 1, wherein the condition is Type II diabetes.

30. (Previously Presented) The method of claim 1, wherein the condition is ischemic diseases of the heart, kidney, liver or brain.

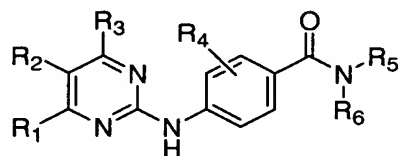
31. (Previously Presented) The method of claim 1, wherein the condition is osteoporosis.

32. (Previously Presented) The method of claim 1, wherein the condition is cachexia.

33. (Previously Presented) The method of claim 1, wherein the condition is transplant rejection, graft versus host disease, endotoxin shock or multiple organ failure.

34-45. (Canceled)

46. (New) A method of inhibiting JNK in a cell expressing JNK, comprising contacting a cell with an effective amount of a compound having the structure:



or a pharmaceutically acceptable salt thereof,
wherein:

R₁ is aryl or heteroaryl optionally substituted with one to four substituents independently selected from R₇;

R₂ and R₃ are the same or different and are independently hydrogen or lower alkyl;

R₄ represents one to four optional substituents, wherein each substituent is the same or different and independently is selected from halogen, hydroxy, lower alkyl or lower alkoxy;

R₅ and R₆ are the same or different and independently are -R₈, -(CH₂)_aC(=O)R₉, -(CH₂)_aC(=O)OR₉, -(CH₂)_aC(=O)NR₉R₁₀, -(CH₂)_aC(=O)NR₉(CH₂)_bC(=O)R₁₀, -(CH₂)_aNR₉C(=O)R₁₀, -(CH₂)_aNR₁₁C(=O)NR₉R₁₀, -(CH₂)_aNR₉R₁₀, -(CH₂)_aOR₉, -(CH₂)_aSO_cR₉, or -(CH₂)_aSO₂NR₉R₁₀;

or R₅ and R₆ taken together with the nitrogen atom to which they are attached to form a heterocycle or substituted heterocycle;

R₇ is at each occurrence independently halogen, hydroxy, cyano, nitro, carboxy, alkyl, alkoxy, haloalkyl, acyloxy, thioalkyl, sulfinylalkyl, sulfonylalkyl, hydroxyalkyl, aryl, substituted aryl, aralkyl, substituted aralkyl, heterocycle, substituted heterocycle, heterocyclealkyl, substituted heterocyclealkyl, -C(=O)OR₈, -OC(=O)R₈, -C(=O)NR₈R₉, -C(=O)NR₈OR₉, -SO_cR₈, -SO_cNR₈R₉, -NR₈SO_cR₉, -NR₈R₉, -NR₈C(=O)R₉, -NR₈C(=O)(CH₂)_bOR₉, -NR₈C(=O)(CH₂)_bR₉, -O(CH₂)_bNR₈R₉, or heterocycle fused to phenyl;

R₉, R₁₀ and R₁₁ are the same or different and at each occurrence are independently hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, aralkyl, substituted arylalkyl, heterocycle, substituted heterocycle, heterocyclealkyl or substituted heterocyclealkyl;

R₈ is aryl, substituted aryl, aralkyl, substituted arylalkyl, heterocycle, substituted heterocycle, heterocyclealkyl or substituted heterocyclealkyl;

or R₈ and R₉ taken together with the atom or atoms to which they are attached to form a heterocycle or substituted heterocycle;

a and *b* are the same or different and at each occurrence independently are selected from 0, 1, 2, 3 or 4; and

c is at each occurrence 0, 1 or 2.